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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,774	05/14/2001	Wolf-Bernd Frommer	514413-3550.1	8393

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	**PAPER NUMBER**
1638	7

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/854,774	FROMMER, WOLF-BERND	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-58* is/are pending in the application.

4a) Of the above claim(s) *29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-28 and 31-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08362512* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the methods of Group II are dependent method claims, directed to a method of using the product of the Group I claims. This is not found persuasive because the DNA of Group I and the hybridization method of Group II, differ because the DNA of Group I can be used in a method other than the method of Group II such as a method of transformation. Also, the transformation method of Group I and the hybridization method of Group II differ in starting material, method steps, and products. The requirement for election of either SEQ ID NO: 1 or SEQ ID NO: 3 has been reconsidered and withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

The specification is objected to under 37 CFR 1.821(d) for not assigning each sequence a unique sequence identifier. Pages 5-9 disclose two sequences, a nucleic acid and a protein, under a single sequence number. Pages 9-14 do the same. It appears that the sequence of SEQ ID NO: 1 on pages 5-9 correspond to SEQ ID NOs: 1 and 2 in the Sequence Listing, and that the sequences of SEQ ID NO: 2 on pages 9-14 correspond to SEQ ID NOs: 3 and 4 in the Sequence Listing. The specification should be amended to correct this inconsistency. See also page 22 of the specification, line 10, which characterizes a plasmid as containing a protein sequence (SEQ ID NO: 2), if the Sequence Listing designations were followed. See also page 24 of the specification, lines 22 and 25.

Furthermore, SEQ ID NOs: 3 and 4 were not discussed in the German priority document. Accordingly, the effective filing date of claims 56 and 58 is 1 July 1993, the filing date of the PCT application in which they were first disclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-28 and 31-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21-28 and 31-54 are broadly drawn to isolated DNA molecules from any plant species, including divergent species such as corn, palm, tobacco, pine, oak, orchid, and soybean, of any sequence. Claims 55-58 are broadly drawn to isolated polynucleotides that encode a plant amino acid transporter and hybridize to either SEQ ID NO: 1 or SEQ ID NO: 3 under conditions of unspecified stringency.

Applicant only describes polynucleotides SEQ ID NO: 1 and SEQ ID NO: 3 that encode plant amino acid transporters from *Arabidopsis* comprising SEQ ID NO: 2 and 4.

Applicant does not describe any other isolated polynucleotides encoding plant amino acid transporters other than SEQ ID NO: 1 and SEQ ID NO: 3 from *Arabidopsis*. Therefore, it is not clear that Applicant was in possession of the invention as broadly claimed.

See *University of California V. Eli Lilly and Co.,* 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Claims 54 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the yeast strains 22574d and JT16 are required to practice the claimed invention. The specification does not provide a repeatable method for obtaining said materials and they do not appear to be readily available materials. Without a publicly available deposit of the above, one of ordinary skill in the art could not be assured of the ability to make plant transformed with a plant amino acid transporter in the same manner as claimed. Given the lack of guidance in the specification and inability of those in the art to reproduce specific yeast mutants, it would require undue experimentation for one skilled in the art to identify and obtain the original mutants of yeast. If it is not so obtainable or available, the enablement requirements

of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of yeast strains 22574d and JT16. See 37 CFR 1.802.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

(a) during the pendency of this application, access to the deposits will be afforded to one determined by the commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in the public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposits will be replaced if they should become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.801 - 1.809 [MPEP 2401-2411.05] for additional explanation of these requirements.

Claims 21-28 and 31-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims isolated DNA molecules from any plant species, including divergent species such as corn, palm, tobacco, pine, oak, orchid, and soybean, of any sequence and isolated polynucleotides that encode a plant amino acid transporter; an isolated DNA molecule that hybridizes to either SEQ ID NO: 1 or SEQ ID NO: 3 under conditions of unspecified stringency; and an isolated DNA molecule that complements a yeast transport mutation.

Applicant teaches isolation of the polynucleotides of SEQ ID NO: 1 and SEQ ID NO: 3 by yeast complementation of yeast strain 22574d deficient in proline transport and yeast strain JT16 deficient in histidine transport (Examples 1-2 pages 23-25); amino acid uptake in yeast complemented with SEQ ID NO: 1 (22574d::pPPP1-20) and SEQ ID NO: 3 (22573d::AAP2) (Example 3 page 25); tobacco transformed with the coding region of SEQ ID NO: 1 (pPPP1-20);

amino acid uptake in yeast complemented with SEQ ID NO: 2 (JT16::AAP2) (Example 5 page 26-27).

Applicant does not teach any other polynucleotide encoding a plant amino acid transporter isolated by yeast complementation, or otherwise, other than SEQ ID NO: 1 and 3; plants transformed with a polynucleotide encoding an amino acid transporter other than tobacco; and any plant transformed with a polynucleotide encoding an amino acid transporter showing either an elevated or decreased level of any amino acid.

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe.

Yeast complementation showed an unexpected result when a putative plant amino acid transporter failed to complement the JT16 yeast mutant originally used to isolate the AAP1 amino acid transporter. In this case the putative amino acid transporter encoded an Arg

transporter, an amino acid that was supplemented in the selection medium, leading to toxic levels of Arg in the complemented mutant when grown in the prescribed selection medium (Chen L. *et al.*, Plant Physiology, 2001, Vol. 125, pp. 1813-1820; page 1814 column 1, lines 2-27).

The unpredictability in understanding how to use the genes for amino acid transport in plants is predicated upon the presence of multiple gene families encoding amino acid transporters that have similar sequence or protein identity (Chen L. *et al.*, Plant Physiology, 2001, Vol. 125, pp. 1813-1820; page 1817, see Figure 6) yet show different specificities for acidic, basic, and neutral amino acids as well as tissue specificity possibly due to a pH or cofactor preference supplied by the specific tissue (Neelam A. *et al.*, Plant Physiology, August 1999, Vol. 120, pp. 1049-1056; page 1055 column 2, beginning second full paragraph to page 1056). Furthermore, [redacted] the lack of understanding of the mechanisms that regulate amino acid content in a plant are characterized in experiments where transgenic plants designed to have an increased amount of lysine were limited in their accumulation of the amino acid because of an increase in the lysine breakdown even though the flux through the pathway had been increased, thereby suggesting that there are unforeseen mechanisms of product accumulation awaiting those of skill in the art (Broun P. *et al.*, PNAS 2001, Vol. 98, no. 16, pp. 8925-8927; page 8926 column 2 lines 40-47).

Moreover, the phenotypic character expected from expression of a DNA construct often cannot be reliably predicted. In an example that demonstrates this all too common and unpredictable feature in the art, antisense expression of a polygalacturonase gene in transgenic tomato had no effect on fruit softening (Smith C. *et al.*; Nature 334: 724-726, 1988, p. 725).

Given the lack of guidance for isolating any plant amino acid transporter from any plant source and for isolating polynucleotide sequences that hybridize to SEQ ID NO: 1, SEQ ID NO: 3, or any essential or conserved sequence thereof under any hybridization conditions, and the lack of guidance with respect to isolating other plant amino acid transporters by complementation to other mutants of yeast deficient in amino acid synthesis and uptake, with consideration of the limited working examples in the specification, the breadth of the claims, and the unpredictability in the art, undue trail and error experimentation would have been required by one skilled in the art to identify and isolate a multitude of non-exemplified polynucleotide sequences encoding plant amino acid transporters, for transformation of a myriad of non-exemplified plant species. Thus, the claims are not enabled.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-28 and 31-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 5,719,043. Although the conflicting claims are not identical, they are not patentably distinct from each other

because the claims of the instant application are broadly drawn to isolated DNA molecules encoding plant amino acid transporters including those hybridizing to *Arabidopsis* derived SEQ ID NO: 1 and 3, plasmids and host cells comprising said DNA molecules, plants transformed with plant amino acid transporter DNA having altered amino acid transporter activity and methods thereof. Thus, the embodiments of the inventions of Claims 1-22 of U.S. Patent 5,719,043 drawn to isolated DNA molecules comprising SEQ ID NOs: 1 and 3, products containing them, and methods of their use, fall within the scope of Claims 21-28, 31-53, and 55-58 of the instant application.

Claims 21-28 and 31-58 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,245,970. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are broadly drawn to isolated DNA molecules encoding plant amino acid transporters including those hybridizing to *Arabidopsis* derived SEQ ID NO: 1 and 3, plasmids and host cells comprising said DNA molecules, plants transformed with plant amino acid transporter DNA having altered amino acid transporter activity and methods thereof. Thus, the embodiments of the inventions of Claims 1-25 of U.S. Patent 6,245,970 B1 fall within the scope of Claims 21-28 and 31-51 of the instant application.

Claims 21-28 and 31-58 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide encoding a plant amino acid transporter and plants transformed with said polynucleotide.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.
November 13, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638